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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,384	08/20/2002	Maria Laura Gennaro	07763-042001	7084

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EXAMINER	
SWARTZ, RODNEY P	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,384	GENNARO	
	Examiner	Art Unit	
	Rodney P. Swartz, Ph.D.	1645	

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21January2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *21-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-36* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RP

DETAILED ACTION

1. Applicants' Response to Restriction Requirement, received 21January2005, is acknowledged. Applicants elect, without traverse, Invention I, claims 1-20, drawn to DNA, vector, transformed cells, polypeptides, and a first method of use for diagnosis *in vivo*.

2. Claims 1-36 are pending. Claims 21-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

3. Claims 1-20 are under consideration.

Specification

4. Applicants are directed to MPEP §608.01(p) for procedures in the event that the instant application is allowed. The following is a recitation of the pertinent paragraph:

> Prior to allowance of an application that incorporates essential material by reference to a pending U.S. application, the examiner shall determine if the referenced application has issued as a patent. If the referenced application has issued as a patent, the examiner shall enter the U.S. Patent No. of the referenced application in the specification of the referencing application (see MPEP§1302.04). If the referenced application has not issued as a patent, applicant will be required to amend the disclosure of the referencing application to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating the amendatory material consists of the same material incorporated by reference in the referencing application.

The specification recites incorporation by reference of U.S. Pat. Appl. 08/796,792 (page 1, lines 16-17; page 13, lines 14-15).

5. The disclosure (page 13, line 32; page 14, lines 6-23) is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

6. The disclosure is objected to because of the following informalities:

Page 20, line 1, "Presence mtsp" should be "Presence of mtsp"

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 9 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acid sequences, does not reasonably provide enablement for vaccines. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention is a vaccine composition comprising $\geq$2 DNA sequences encoding *M. tuberculosis* polypeptides.

The state of the prior art as evidenced by the attached references indicates that successful subunit vaccine compositions of mycobacterial DNA or polypeptides lacks predictability. Whether a particular vaccine composition results in protection against mycobacterial infection necessitates actual testing *in vivo* in animals and/or humans. To date, the only successful vaccine composition for use in humans is *M. bovis* BCG.

The amount of direction or guidance present in the instant specification is merely speculative concerning the isolated DNA sequences and encoded polypeptides. The only examples present in the instant specification are computer generated sequences of *M. tuberculosis* DNA and predicted *M. tuberculosis* proteins. The specification does not contain any examples, in test animals or in humans, of the claimed vaccines.

The quantity of experimentation necessary for one of skill in the art to produce vaccine compositions which are effective in protecting hosts against infection with *M. tuberculosis* constitutes merely an invitation to experiment without a reasonable expectation of success.

9. Claims 17-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for predicted polypeptide sequences, does not reasonably provide enablement for diagnostic methods utilizing the polypeptide sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction

or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention is a method of diagnosis of a subject that has or is susceptible to infection with *M. tuberculosis* comprising administration to a subject a polypeptide composition and detecting an immune response.

The state of the prior art concerning diagnosis of *M. tuberculosis* infected hosts or hosts susceptibility to *M. tuberculosi s* is improving. However, there is a lack of predictability in the art *a priori* concerning the success in diagnosis utilizing subunit polypeptides for detecting if a host is infected with or susceptibility to *M. tuberculosis*, see attached Review( ).

The amount of direction or guidance present in the specification is merely speculative concerning success of an individual polypeptide as a diagnostic composition in methods for specifically detecting *M. tuberculosis* infected hosts or hosts susceptibility to *M. tuberculosis.*

The specification contains no working examples of methods for detecting *M. tuberculosis* infected hosts or hosts susceptibility to *M. tuberculosis* utilizing the listed polypeptides or any other compositions. The specification merely contains computer generated sequences of *M. tuberculosis* DNA and predicted *M. tuberculosis* proteins.

Therefore, the quantity of experimentation necessary by one of skill in the art to determine if any of the listed polypeptides, alone or in combinations, is efficacious for specifically detecting *M. tuberculosis* infected hosts or hosts susceptibility to *M. tuberculosis* constitutes merely an invitation to experiment without a reasonable expectation of success.

10. Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to *M. tuberculosis* DNA, vectors, transformed cells, polypeptides, and a method of diagnosis utilizing polypeptides wherein the amino acid sequence encoded by said DNA is identical to MTSP1-47 but with conservative substitutions. There is no limit on the number of conservative substitutions. The claims also recite that such polypeptides have *M. tuberculosis* specific antigenic and immunogenic properties. However, the specification does not provide guidance concerning the number of residues nor which residues can be conservatively substituted and yet allow the polypeptide to retain *M. tuberculosis* specific antigenic and immunogenic properties. While the specification teaches various DNA sequences which appear in a variety of *Mycobacteria*, the specification does not provide guidance to which sequences and resulting polypeptides have the claimed *M. tuberculosis* specific antigenic and immunogenic properties.

Therefore, the claims are indefinite concerning: 1) *M. tuberculosis* specific antigenic and immunogenic properties required, and 2) the number of residues nor the identity of which residues can be conservatively substituted and yet allow the polypeptide to retain *M. tuberculosis* specific antigenic and immunogenic properties.

Conclusion

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rodney P. Swartz, Ph.D., Art Unit 1645, whose telephone number is (571)

272-0865. The examiner can normally be reached on Monday through Thursday from 5:30 AM to 4:00 PM EST.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F. Smith, can be reached on (571)272-0864.

The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER
Art Unit 1645

April 30, 2005